

## Supplementary Appendix

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**SUPPLEMENTARY APPENDIX**  
**DEMOGRAPHIC AND EPIDEMIOLOGIC DRIVERS OF GLOBAL CARDIOVASCULAR MORTALITY**

**Table of Contents**

Mortality Estimation in the Global Burden of Disease Study	Page 2
Supplementary Table S1. Global Burden of Disease Analytic Regions	Page 5
Supplementary Appendix References	Page 18

## **Mortality Estimation in the Global Burden of Disease Study**

The Global Burden of Disease (GBD) approach to estimating all-cause mortality and cause-specific mortality has been previously described.<sup>1,2</sup> For GBD 2010, we defined 291 causes of death or disability of which 235 are causes of death; this cause list was developed using an extensive database of vital registration records, verbal autopsy data, burial and mortuary data, in-hospital death records, police reports, census records, and registries. For GBD 2013 we have expanded the cause list to include 303 causes, of which 240 are causes of death. Of these causes, 11 are cardiovascular (see Table 1 in the main article). Causes of death are stratified into three different levels based on specificity of cause; for example, “cardiovascular and circulatory diseases” is a level 1 classification; “cerebrovascular disease” is a level 2 classification under “cardiovascular and circulatory diseases;” and “ischemic stroke” is a level 3 classification under “cerebrovascular disease.”

We divided the countries of the world into 21 regions and seven super-regions as defined in the GBD 2010. The GBD 2013 also includes an assessment of subnational populations in three countries: provinces for China, states for Mexico, and the United Kingdom broken down into Scotland, Wales, Northern Ireland, and nine regions of England. These countries have been analyzed at the sub-national level because of the interest of national collaborators and because sufficient data were made available by teams in each country. The full list of analytic regions and countries or subnational regions is provided in Supplementary Appendix Table S1.

## **Covariates**

National-level time series (from 1980 to 2013) for a wide range of covariates were estimated based on data from available survey microdata, censuses, official reports, administrative data, as well as systematic literature review. For lagged distributed income and education, national-level time series were estimated from 1950 to 2013. Details on the data and methods used to generate the imputed series for GDP, educational attainment, tobacco prevalence and obesity prevalence have been published.<sup>3–6</sup>

## **All-cause Mortality**

Because vital registration systems do not exist in all countries, measurement of mortality requires use of multiple sources of data and application of appropriate methods of extrapolation. Following the GBD 2010 methods, we systematically identified all available vital registration data, sibling history survey data, sample registration data, and household recall of deaths. Vital registration data were evaluated for completeness using optimized death distribution methods.<sup>1,7</sup> Sibling history data were analyzed to account for survivor bias, zero-surviving sibships, and recall bias.<sup>1,8</sup> All sources are synthesized using the combination of spatio-temporal regression and Gaussian Process Regression (GPR). The mean function for the GPR is based on the combination of a non-linear hierarchical model with income per capita, mean years of education in age group 15 to 60, mortality rate due to HIV/AIDS, and country random effects<sup>1</sup> as covariates, and a spatio-temporal regression where we add to the first stage model without country random effects the smoothed residuals between the first stage model and observed data. For further details, please see reference 9.

The GBD 2010 introduced a model life table system to estimate the full age pattern of mortality for country-years of interests.<sup>10</sup> For GBD 2013, we have modified how the standard mortality schedule is selected for each country-year so that the same approach is used for all countries. Specifically, we compute empirically a set of space-time weights that relate the observed age pattern of the probability of death in a sex-country-year with other sex-country-year observations. Age and sex-specific death rates from the life table are used to generate death numbers by multiplying by population estimates from the World Population Prospects 2012 revision and the Human Mortality Database for age groups higher than age five.<sup>11</sup> For the under-five age groups, we apply the method developed by Wang et al.<sup>10</sup>

### **Modeling of Individual Causes of Death**

As in the GBD 2010, we used six different modeling strategies for causes of death depending on the strength of the available data. For cardiovascular causes of death, we used cause of death ensemble modeling (CODEm). CODEm has been extensively used in global health estimation including the GBD 2010.<sup>2,12,13</sup> The advantage is that a wide range of different models are tested. Only models meeting predetermined criteria in terms of the statistical significance and direction of regression coefficients are retained. 30% of the data are held out of the initial analysis so that the performance of different models is assessed in terms of how well they predict the data held out. Through multiple iterations of the hold-out process (cross-validation), stable objective information on model performance is obtained. The best performing models in terms of root-mean squared error for level and trend are combined into a model ensemble.

### **Combining Results for Individual Causes of Death**

In the GBD 2010, because single-cause models were developed for each cause, the final step was to combine these models into estimates that are consistent with all-cause mortality for each age-sex-country-year group. To reconcile the difference between the sum of the deaths from individually modeled diseases and our overall mortality levels, we used an algorithm developed by the GBD study and designated CoDCorrect. The CoDCorrect process is intended to take into account uncertainty both in the all-cause mortality envelope and uncertainty in the estimates for each cause.

For each cause-specific model and for all-cause mortality, we had 1000 draws from the posterior distribution for each age-sex-country-year group. We combined causes by taking a random draw without replacement from the posterior distribution of each cause and all-cause mortality. Each cause was rescaled by a scalar equal to the draw of all-cause mortality divided by the sum of the draws of individual causes. GBD 2010 induced a correlation of 1.0 between the sum of cause-specific and all-cause mortality. CoDCorrect was applied in a hierarchical fashion: first to level 1 causes and then to level 2 and level 3 causes. Level two causes were constrained to sum to the level 1 parent cause. Levels of this cascade were largely the same as used in GBD 2010 and were chosen based on consideration of the amount and quality of available cause of death data.

For GBD 2013, we have made slight modifications to this approach. Because testing showed no substantial effect of the 1.0 correlation between draws of all-cause mortality and the sum of individual

causes and because each cause is modeled independently such that the ordering of draws across causes are unrelated, we have removed this assumption. We also made some adjustments in the way HIV deaths are handled, as described in reference 9.

SUPPLEMENTARY APPENDIX TABLE S1. Global Burden of Disease Analytic Regions

<b>Region</b>	<b>Country or Subnational Region</b>
Andean Latin America	Bolivia
Andean Latin America	Ecuador
Andean Latin America	Peru
Australasia	Australia
Australasia	New Zealand
Caribbean	Anguilla
Caribbean	Antigua and Barbuda
Caribbean	Aruba
Caribbean	Barbados
Caribbean	Belize
Caribbean	Bermuda
Caribbean	Cayman Islands
Caribbean	Cuba
Caribbean	Dominica
Caribbean	Dominican Republic
Caribbean	French Guiana
Caribbean	Grenada
Caribbean	Guadeloupe
Caribbean	Guyana
Caribbean	Haiti
Caribbean	Jamaica
Caribbean	Martinique
Caribbean	Montserrat

Caribbean	Netherlands Antilles
Caribbean	Puerto Rico
Caribbean	Saint Barthelemy
Caribbean	Saint Kitts and Nevis
Caribbean	Saint Lucia
Caribbean	Saint Martin
Caribbean	Saint Vincent and the Grenadines
Caribbean	Suriname
Caribbean	The Bahamas
Caribbean	Trinidad and Tobago
Caribbean	Turks and Caicos Islands
Caribbean	Virgin Islands, British
Caribbean	Virgin Islands, U.S.
Central Asia	Armenia
Central Asia	Azerbaijan
Central Asia	Georgia
Central Asia	Kazakhstan
Central Asia	Kyrgyzstan
Central Asia	Mongolia
Central Asia	Tajikistan
Central Asia	Turkmenistan
Central Asia	Uzbekistan
Central Europe	Albania
Central Europe	Bosnia and Herzegovina
Central Europe	Bulgaria
Central Europe	Croatia

Central Europe	Czech Republic
Central Europe	Hungary
Central Europe	Macedonia
Central Europe	Montenegro
Central Europe	Poland
Central Europe	Romania
Central Europe	Serbia
Central Europe	Slovakia
Central Europe	Slovenia
Central Latin America	Aguascalientes
Central Latin America	Baja California
Central Latin America	Baja California Sur
Central Latin America	Campeche
Central Latin America	Chiapas
Central Latin America	Chihuahua
Central Latin America	Coahuila
Central Latin America	Colima
Central Latin America	Colombia
Central Latin America	Costa Rica
Central Latin America	Distrito Federal
Central Latin America	Durango
Central Latin America	El Salvador
Central Latin America	Guanajuato
Central Latin America	Guatemala
Central Latin America	Guerrero
Central Latin America	Hidalgo



Central Latin America	Honduras
Central Latin America	Jalisco
Central Latin America	Mexico
Central Latin America	México
Central Latin America	Michoacán de Ocampo
Central Latin America	Morelos
Central Latin America	Nayarit
Central Latin America	Nicaragua
Central Latin America	Nuevo León
Central Latin America	Oaxaca
Central Latin America	Panama
Central Latin America	Puebla
Central Latin America	Querétaro
Central Latin America	Quintana Roo
Central Latin America	San Luis Potosí
Central Latin America	Sinaloa
Central Latin America	Sonora
Central Latin America	Tabasco
Central Latin America	Tamaulipas
Central Latin America	Tlaxcala
Central Latin America	Venezuela
Central Latin America	Veracruz de Ignacio de la Llave
Central Latin America	Yucatán
Central Latin America	Zacatecas
Central Sub-Saharan Africa	Angola
Central Sub-Saharan Africa	Central African Republic

Central Sub-Saharan Africa	Congo
Central Sub-Saharan Africa	Democratic Republic of the Congo
Central Sub-Saharan Africa	Equatorial Guinea
Central Sub-Saharan Africa	Gabon
East Asia	Anhui
East Asia	Beijing
East Asia	China
East Asia	Chongqing
East Asia	Fujian
East Asia	Gansu
East Asia	Guangdong
East Asia	Guangxi
East Asia	Guizhou
East Asia	Hainan
East Asia	Hebei
East Asia	Heilongjiang
East Asia	Henan
East Asia	Hong Kong Special Administrative Region of China
East Asia	Hubei
East Asia	Hunan
East Asia	Inner Mongolia
East Asia	Jiangsu
East Asia	Jiangxi
East Asia	Jilin

East Asia	Liaoning
East Asia	Macao Special Administrative Region of China
East Asia	Ningxia
East Asia	North Korea
East Asia	Qinghai
East Asia	Shaanxi
East Asia	Shandong
East Asia	Shanghai
East Asia	Shanxi
East Asia	Sichuan
East Asia	Taiwan
East Asia	Tianjin
East Asia	Tibet
East Asia	Xinjiang
East Asia	Yunnan
East Asia	Zhejiang
Eastern Europe	Belarus
Eastern Europe	Estonia
Eastern Europe	Latvia
Eastern Europe	Lithuania
Eastern Europe	Moldova
Eastern Europe	Russia
Eastern Europe	Ukraine
Eastern Sub-Saharan Africa	Burundi
Eastern Sub-Saharan Africa	Comoros

Eastern Sub-Saharan Africa	Djibouti
Eastern Sub-Saharan Africa	Eritrea
Eastern Sub-Saharan Africa	Ethiopia
Eastern Sub-Saharan Africa	Kenya
Eastern Sub-Saharan Africa	Madagascar
Eastern Sub-Saharan Africa	Malawi
Eastern Sub-Saharan Africa	Mozambique
Eastern Sub-Saharan Africa	Rwanda
Eastern Sub-Saharan Africa	Somalia
Eastern Sub-Saharan Africa	South Sudan
Eastern Sub-Saharan Africa	Tanzania
Eastern Sub-Saharan Africa	Uganda
Eastern Sub-Saharan Africa	Zambia
High-income Asia Pacific	Brunei
High-income Asia Pacific	Japan
High-income Asia Pacific	Singapore
High-income Asia Pacific	South Korea
High-income North America	Canada
High-income North America	Saint Pierre and Miquelon
High-income North America	United States
North Africa and Middle East	Afghanistan
North Africa and Middle East	Algeria
North Africa and Middle East	Bahrain
North Africa and Middle East	Egypt
North Africa and Middle East	Iran
North Africa and Middle East	Iraq

North Africa and Middle East	Jordan
North Africa and Middle East	Kuwait
North Africa and Middle East	Lebanon
North Africa and Middle East	Libya
North Africa and Middle East	Morocco
North Africa and Middle East	Oman
North Africa and Middle East	Palestine
North Africa and Middle East	Qatar
North Africa and Middle East	Saudi Arabia
North Africa and Middle East	Sudan
North Africa and Middle East	Syria
North Africa and Middle East	Tunisia
North Africa and Middle East	Turkey
North Africa and Middle East	United Arab Emirates
North Africa and Middle East	Western Sahara
North Africa and Middle East	Yemen
Oceania	American Samoa
Oceania	Cook Islands
Oceania	Federated States of Micronesia
Oceania	Fiji
Oceania	French Polynesia
Oceania	Guam
Oceania	Kiribati
Oceania	Marshall Islands
Oceania	Nauru
Oceania	New Caledonia

Oceania	Niue
Oceania	Norfolk Island
Oceania	Northern Mariana Islands
Oceania	Palau
Oceania	Papua New Guinea
Oceania	Pitcairn Islands
Oceania	Samoa
Oceania	Solomon Islands
Oceania	Tokelau
Oceania	Tonga
Oceania	Tuvalu
Oceania	Vanuatu
Oceania	Wallis and Futuna Islands
South Asia	Bangladesh
South Asia	Bhutan
South Asia	India
South Asia	India, Rural
South Asia	India, Urban
South Asia	Nepal
South Asia	Pakistan
Southeast Asia	Cambodia
Southeast Asia	Christmas Island
Southeast Asia	Cocos (Keeling) Islands
Southeast Asia	Indonesia
Southeast Asia	Laos
Southeast Asia	Malaysia

Southeast Asia	Maldives
Southeast Asia	Mauritius
Southeast Asia	Myanmar
Southeast Asia	Philippines
Southeast Asia	Reunion
Southeast Asia	Seychelles
Southeast Asia	Sri Lanka
Southeast Asia	Thailand
Southeast Asia	Timor-Leste
Southeast Asia	Vietnam
Southern Latin America	Argentina
Southern Latin America	Chile
Southern Latin America	Falkland Islands (Islas Malvinas)
Southern Latin America	Uruguay
Southern Sub-Saharan Africa	Botswana
Southern Sub-Saharan Africa	Eastern Cape
Southern Sub-Saharan Africa	Free State
Southern Sub-Saharan Africa	Gauteng
Southern Sub-Saharan Africa	KwaZulu-Natal
Southern Sub-Saharan Africa	Lesotho
Southern Sub-Saharan Africa	Limpopo
Southern Sub-Saharan Africa	Mpumalanga
Southern Sub-Saharan Africa	Namibia
Southern Sub-Saharan Africa	Northern Cape
Southern Sub-Saharan Africa	North-West
Southern Sub-Saharan Africa	South Africa

Southern Sub-Saharan Africa	Swaziland
Southern Sub-Saharan Africa	Western Cape
Southern Sub-Saharan Africa	Zimbabwe
Tropical Latin America	Brazil
Tropical Latin America	Paraguay
Western Europe	Akrotiri and Dhekelia
Western Europe	Aland Islands
Western Europe	Andorra
Western Europe	Austria
Western Europe	Belgium
Western Europe	Channel Islands
Western Europe	Cyprus
Western Europe	Denmark
Western Europe	East Midlands
Western Europe	East of England
Western Europe	England
Western Europe	Faroe Islands
Western Europe	Finland
Western Europe	France
Western Europe	Germany
Western Europe	Gibraltar
Western Europe	Greater London
Western Europe	Greece
Western Europe	Greenland
Western Europe	Guernsey
Western Europe	Holy See (Vatican City)



Western Europe	Iceland
Western Europe	Ireland
Western Europe	Isle of Man
Western Europe	Israel
Western Europe	Italy
Western Europe	Jersey
Western Europe	Liechtenstein
Western Europe	Luxembourg
Western Europe	Malta
Western Europe	Monaco
Western Europe	Netherlands
Western Europe	North East England
Western Europe	North West England
Western Europe	Northern Ireland
Western Europe	Norway
Western Europe	Portugal
Western Europe	San Marino
Western Europe	Scotland
Western Europe	South East England
Western Europe	South West England
Western Europe	Spain
Western Europe	Svalbard and Jan Mayen Islands
Western Europe	Sweden
Western Europe	Switzerland
Western Europe	United Kingdom
Western Europe	Wales

Western Europe	West Midlands
Western Europe	Yorkshire and the Humber
Western Sub-Saharan Africa	Benin
Western Sub-Saharan Africa	Burkina Faso
Western Sub-Saharan Africa	Cameroon
Western Sub-Saharan Africa	Cape Verde
Western Sub-Saharan Africa	Chad
Western Sub-Saharan Africa	Cote d'Ivoire
Western Sub-Saharan Africa	Ghana
Western Sub-Saharan Africa	Guinea
Western Sub-Saharan Africa	Guinea-Bissau
Western Sub-Saharan Africa	Liberia
Western Sub-Saharan Africa	Mali
Western Sub-Saharan Africa	Mauritania
Western Sub-Saharan Africa	Niger
Western Sub-Saharan Africa	Nigeria
Western Sub-Saharan Africa	Saint Helena
Western Sub-Saharan Africa	Sao Tome and Principe
Western Sub-Saharan Africa	Senegal
Western Sub-Saharan Africa	Sierra Leone
Western Sub-Saharan Africa	The Gambia
Western Sub-Saharan Africa	Togo

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